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## REMARKS

Claim 12 is pending in the present application. New claims 27-29 have been added. New claims 27-29 find their support starting in the last paragraph of page 4 through page 5 of the specification. No new matter has been added. Upon entry of the present amendment, claims 12 and 27-39 will be pending.

## I. Summary of the Claimed Invention

Applicants' invention is directed to, *inter alia*, a method of identifying a *virtual* compound in a library of compounds by 1) dissecting the compounds into constituent fragments, 2) adding the constituent fragments together in sequential synthesis rounds, 3) tracking the virtual synthetic addition of the constituent fragments, and 4) identifying each compound member of the library by the synthetic method, constituent fragments and associated reagents. The constituent fragment is associated with at least one reagent which represents a necessary chemical to introduce the fragment into the compound. The dissecting is based on the ease of synthesis of the compound from the constituent fragments. Thus, the method identifies constituent fragments that, together, provide a part of the retrosynthetic analysis of the compound. This method is amply described, for example, starting at about page 4 of the present application where Applicants teach:

According to the methods of the present invention, each compound or library member is dissected into its component or constituent parts referred to as fragments. Thus each compound that is generated is considered to be comprised of constituent fragments such that the sum of the molecular formulas of each of the fragments when added together totals the molecular formula of the compound generated. This dissection can be done in a variety of ways using chemical intuition.

Thus, the compound to be identified is dissected into constituents, which are then recombined *in silico* according to the synthetic method. The compounds are thereby identified according to its synthetic method, constituent fragments and associated reagents. The unique identity of each compound is thereby determined according to the methods of the present invention.

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**II. Obviousness-Type Double Patenting**

Claim 12 is rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 8 and 9 of U.S. Patent No. 6,253,168 (the "168 patent"). Applicants traverse this rejection and respectfully request reconsideration because the claimed invention is not an obvious variation of the subject matter recited in claims 8 or 9 of the 168 patent.

Claim 8 of the 168 patent recites:

A method of generating a database comprising information about the member compounds of a virtual library of compounds comprising:

selecting each of said compounds for said virtual library and, for each, dissecting each of said compounds into fragments; linking together the fragments of each of the compounds; tracking the sequence of linkage for each compound; grouping two or more compounds of said library together to form a mixture;

grouping a further two or more compounds of said library together to form a further mixture;

linking together the tracked information of each of the members of said mixture;

linking together the tracked information of each of the members of said further mixture; and

storing said tracked information thereby generating a database.

Claim 9 of the 168 patent recites:

A method of generating a database comprising information about member compounds in a virtual library of compounds comprising:

selecting each of said compounds for said virtual library and, for each, dissecting said compounds into fragments;

representing each of said fragments as a transformation wherein each transformation is a one to one link between a fragment and a reagent used to introduce said fragment into one of said compounds;

linking together the transformations of each of the compounds;

tracking the sequence of linkage for each compound; and

storing said transformation information thereby generating a database.

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Claims 8 and 9 of the 168 patent recite an increased number of steps and recite different features as compared to claim 12 of the present invention. The Examiner admits that the claims of the 168 patent do NOT address identifying *in silico* compounds (rejection of 12/30/2003, pages 4-5). The examiner therein asserts that the process of generating the database, "... will, therefore obviously describe the member compound ...". Applicants disagree with this assertion. What the Examiner appears to suggest is that simply because a method claimed by the present patent application may be modified in such a way as also to be within a claim or claims of a co-pending patent application, an obviousness-type double patenting rejection is warranted. However, this is not the law. An obviousness-type double patenting rejection is analogous to a failure to meet the nonobviousness requirement of 35 U.S.C. §103. *In re Braithwaite*, 154 U.S.P.Q. 29, 34 (C.C.P.A. 1967) and *In re Longi*, 225 U.S.P.Q. 645, 648 n.4 (Fed. Cir. 1985). Thus, under the law, the pivotal question in an obviousness-type double patenting analysis is: Does any claim in the application define merely an obvious variation of an invention disclosed and claimed in the patent? *In re Vogel*, 164 U.S.P.Q. 619 (C.C.P.A. 1970). If the answer to this question is no, there can be no double patenting. In making this analysis, then, the proper inquiry is as taught in *Graham v. John Deere Co.*, 383 U.S. 1 (1966). See, M.P.E.P. §804. The patent laws require more than a mere overlap in claim scope when concluding that particular compounds are obvious variants. As stated by the Federal Circuit:

The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious. (citation omitted).

*In re Baird*, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994). As stated in §804 of the M.P.E.P., the analysis employed in an obvious-type double patenting determination parallels the guidelines for analysis of a 35 U.S.C. §103 rejection, which requires analysis of the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1 (1966). No such analysis has been carried out in the Office Action.

Moreover, Applicants respectfully submit that this double patenting rejection flies in the face of the restriction requirements issued May 20, 2002 and February 26, 2003. In the restriction requirement of May 20, 2002, the Office stated that claims 12 and 13, directed to methods of identifying compounds, are patentably distinct over claims 14-26, directed to methods of storing

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information. The Office further stated that claims 12 and 13 are patentably distinct over claims 1-6 and 7-11, drawn to generation of a database. Thus, claims 12 and 13 were placed into a different group than claims 1-6, 7-11 and 14-26. Accordingly, the Office previously asserted claim 12 to be non-obvious in view of the claims of the 168 patent. Thus, the obviousness type double patenting rejection is misplaced. The double-patenting rejection is not supported by the 168 claim language and is contradicted by the May 20, 2002 restriction requirement. Accordingly, Applicants respectfully request that this rejection be withdrawn.

### III. The Claimed Invention Is Not Obvious

Claim 12 is rejected under 35 U.S.C. §103(a) as allegedly being obvious over Walters et. al. (DDT, 1998, 3, 160-178; hereinafter "the Walters reference"). The Office Action asserts that it would have been obvious to one skilled in the art to characterize any compound of interest by employing the methods reported in the Walters reference and to further extend such characterization to each compound of the library. Applicants traverse the rejection and respectfully request reconsideration of the same.

The Walters reference does not support a *prima facie* showing of obviousness. Indeed, the Walters reference fails to either teach or suggest identifying a compound through the **dissection** of a compound into constituents and adding the constituents in sequential synthesis rounds. In contrast, the Walters reference is directed to reviewing the state of the art in virtual screening (VS) and more particularly the many problems associated therewith.

The Walters reference on page 168 proceeds to present the two main approaches to solving the problem of VS construction or synthesis of molecules. First, a limitation on the complexity of compounds to be synthesized is explored and second, the unrestricted generation of compounds through computer-aided organic synthesis. In the first instance, the computer is provided a database of starting materials, from which new compounds are to be virtually constructed. In the second instance, a computer analyzes a compound to "determine which compounds could be **readily** synthesized." (emphasis added). In the first instance, the goal and the result is the un-restricted (thereby un-guided) synthesis of new compounds. In the second instance, the computer merely provides the subjective ease at which a compound could be synthesized. This synthetic ease is not determined through dissecting the subject compound into

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constituent fragments and tracking the addition of constituent fragments in sequential synthesis rounds. The computer software is directed to generating graphical representations of potential library members. Importantly, the "Chemically aware" builder referenced by the Office Action does not present components of the virtual library as combinations of reagents and corresponding reactions; but, rather, is a method of providing every permutation and exhaustive combination of synthetic parts. This exhaustive combination is done without tracking the synthetic rounds and with no basis in real-world reactions. The computer is provided a set of building blocks and instructed to combine them in each and every combination. Indeed, Walters discloses the automated formation of virtual chemicals, not the dissection and identification of library members as presently claimed.

In neither synthetic instance in the Walters reference is a compound dissected into constituent fragments. In neither synthetic instance in the Walters reference are constituent fragments added in sequential synthesis rounds; nor is tracking of said synthesis and reaction particulars performed in the Walters reference.

The Office Action further propose that the software "Computer-Aided Estimation of Synthetic Accessibility" evaluates members of the library by their synthesizability, i.e., by their building blocks and chemical reactions among them." Applicants disagree with this conclusion and respectfully submit that the CAESA software merely compares the ease at which the design program was able to synthesis a compound. The Walters reference states at page 169, right hand column, referring to this software:

that is designed to rank the synthesizability of a series of candidate molecules **generated** by a *de novo* design program. CAESA uses a library of **generalized** synthetic transformations in conjunction with an analysis of features such as stereocenters to determine which molecules can be easily synthesized. (Emphasis added)

The CAESA software uses **generalized** synthetic transformations, whereas the present claim is directed to specific transformations. Specifically, the present claim recites the association of constituent fragments with at least one reagent which is necessary to introduce the constituent fragment into the compound. Contrastingly, the CAESA software is directed to determining theoretic ease of synthesis based on an analysis of structural features. CAESA does not dissect

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library members into constituent fragments, nor is there a subsequent adding of constituent fragments, through specific reagents, in sequential synthesis rounds with tracking thereof.

The Office Action states that the characterization of a compound of interest is known to those skilled in the art. However, the present claims are not directed to characterization. In contrast, the present claim is directed to identification. Claim 12 recites that the subject compound be dissected into constituent fragments. The present claim is directed to identifying each compound of the library. The specification provides the following insight into the meaning of the term "identifying."

The identifying characteristics describing each transformation include a 1:1 link (a one to one link) between a fragment and a reagent, and the reaction conditions which include, solvent, concentration, temperature and pressure requirements, or auxiliary reagents necessary to effect the introduction of the fragment into the compound by using an appropriate reagent.

By contrast, characterization is defined by the dictionary to mean:

- 1.-The act or an instance of characterizing.
- 2-A description of qualities or peculiarities: *a list of places of interest, with brief characterizations of each.*
- 3-Representation of a character or characters on the stage or in writing, especially by imitating or describing actions, gestures, or speeches. ( Webster's Unabridged Dictionary, NY; 1989)

Although Walters presents information such as stereocenter, conformational complexity or other peculiarities, there is no teaching of the elements of the present claim. The present claims are not directed to describing the peculiarities of library compounds.

In the present claim, identification provides identification on the selected compound including specific reagents and constituent fragments.

The Walters reference does not disclose methods of compound identification. The Walters reference does not disclose dissecting a compound into constituent fragments. The Walters reference does not disclose adding constituent fragments in sequential synthesis rounds defining thereby a synthetic method for the compound from the constituent fragments.

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In establishing a *prima facie* case of obviousness under 35 U.S.C. §103, it is incumbent upon the Examiner to provide a reason why one of ordinary skill in the art would have been led to modify a prior art reference to arrive at the claimed invention. *Ex parte Clapp*, 227 U.S.P.Q. 972 (Bd. Pat. App. Int. 1985). To this end, the requisite motivation must stem from some teaching, suggestion or inference in the prior art as a whole or from the knowledge generally available to one of ordinary skill in the art and not from appellants' disclosure, see for example, *Uniroyal Inc. v. Rudkin-Wiley Corp.*, 5 U.S.P.Q.2d 1434 (Fed. Cir. 1988); and *Ex parte Nesbit*, 25 U.S.P.Q.2d 1817, 1819 (Bd. Pat. App. Int. 1992). In this respect, the following quotation from *Ex parte Levengood*, 28 U.S.P.Q.2d 1300, 1302 (Pat. Off. Bd. App. 1993), is noteworthy:

Our reviewing courts have often advised the Patent and Trademark Office that it can satisfy the burden of establishing a *prima facie* case of obviousness only by showing some objective teaching in either the prior art, or knowledge generally available to one of ordinary skill in the art, that "would lead" that individual "to combine the relevant teachings of the references." ... Accordingly, an examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force that would impel one skilled in the art to do what the patent applicant has done. (citations omitted; emphasis added)

Significantly, the Office Action identifies no "motivating force" that would "impel" persons of ordinary skill to modify the teachings of the Walters reference and achieve the claimed invention. Indeed, the Office Action has not even identified any motivation to modify the teachings of the Walters reference to 1) dissecting a compound into fragments, and 2) adding constituent fragments in sequential synthesis rounds. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

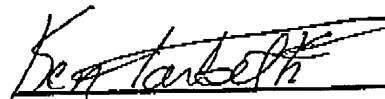
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**IV. Conclusion**

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (619) 685-1708 if there are any questions regarding Applicants' claimed invention.

Respectfully submitted,



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